UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,107	05/23/2005	Charlotta Olsson	1501-1276	5068

466 7590 04/25/2008

YOUNG & THOMPSON
209 Madison Street
Suite 500
ALEXANDRIA, VA 22314

EXAMINER
CROW, ROBERT THOMAS

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
04/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Art Unit: 1634

Attachment

1. For the purpose of appeal, the proposed amendment(s) will be entered and the proposed rejection(s) detailed below will be included in the Examiner's Answer. To be complete, such rejections must be addressed in any brief on appeal.

Status of the Claims

2. Claims 7 and 17-18 were canceled in previous amendments. Claim 9 is cancelled in the instant amendment.

3. Upon entry of the amendment(s) for purposes of appeal:

A. As noted on Form PTO-303 included herein, the previous rejections under 35 USC 112, First Paragraph would be withdrawn in view of Applicant's arguments on pages 7-8 of the Remarks filed 10 April 2008 (i.e., the "Remarks"). As also noted on Form PTO-303, Applicant's amendments would overcome the previous objections to the Specification and the Claims.

B. Claims 1-6, 8, 10, 13, and 16 would be rejected under 35 U.S.C. 103(a) as being unpatentable over Kawashima et al (PCT International Application No. WO 98/44152, published 8 October 1998) in view of Urdea et al (U.S. Patent No. 4,910,300, issued 20 March 1990) for the reasons set forth below.

Regarding claims 1, 10, and 13, Kawashima et al teach a method for determining the sequence of a nucleic acid. In a single exemplary embodiment, Kawashima et al teach providing a single stranded form of a nucleic acid; i.e., a single stranded target nucleic acid (page 5, lines 15-20). The single stranded nucleic acid molecule is then hybridized to a primer to form a template/primer complex (page 5, lines 15-20). The primer is enzymatically extended by addition of a polymerase and extension with at least one nucleotide (page 6, lines 1-5) wherein the at least one nucleotide is a mixture comprising less than 50% of a labeled form of the at least one nucleotide (page 16, lines 15-23). The extension product comprising the

labeled nucleotide is then detected (page 6, lines 6-10); because a given (i.e., single) nucleotide is provided in the extension step (page 6, lines 1-5), the type of nucleotide incorporated is known. The label is neutralized after the detection step by photobleaching; namely, laser bleaching of the fluorophores, which are labels (page 18, lines 13-19). Because labels are periodically photobleached after several extension and detection steps (page 18, lines 13-19 and page 6, lines 23-27), the removal occurs more than once (i.e., "periodically;" page 6, lines 23-27) after at least two repetitions of the detection step. Kawashima et al also teach the extension and detection steps are repeated at least once (page 6, lines 10-15).

It is noted that the open claim language "comprising" in line 2 of the claim encompasses additional steps between extension of the primer and the final part of step c) comprising "thereafter determining the type of nucleotide added to the primer and thereafter neutralizing the label by adding a label-interacting agent or by bleaching repeating steps c) to d) at least once." Thus, after a label is removed by photobleaching (i.e., "step c)" of the instant claims), multiple rounds of enzymatic extension with a mixture of labeled and unlabeled nucleotides and determination of the type of nucleotide added before a subsequent photobleaching step (which constitutes "step d)" of the instant claim) are encompassed by the open claim language "comprising."

While Kawashima et al teach the labels are fluorescent labels (page 7, lines 15-22), and that the labels are removed (page 6, lines 25-26), Kawashima et al do not explicitly teach a cleavable link between the label and the nucleotide (i.e., claim 1) that is a disulfide (i.e., claim 10) and the linker is shorter than 8 atoms (i.e., claim 13). Thus, Kawashima et al teach a method that differs from the instantly claimed method because Kawashima et al do not teach a cleavable link between the label and the nucleotide.

However, Urdea et al teach detectably labeled nucleotides (column 8, lines 20-60), wherein the detectable label is a fluorescent label (column 4, lines 5-10) and is linked to the nucleotide with a cleavable linker in the form of a disulfide linker (i.e., claim 10; column 8, lines 20-60). The linker between the disulfide bridge and the base is less than 8 atoms; namely, Formula 13 has label R1, a disulfide for R2, x is one CH2 linker, and NH connects to the base (i.e., claim 13; column 8, lines 20-60). Urdea et al further

teach that the nucleotides having the linkers and labels have the added advantage of being inexpensively synthesized in large quantity (column 2, lines 15-40). Thus, Urdea et al teach the known technique of using a cleavable link between a label and a nucleotide.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising the use of labeled nucleotides as taught by Kawashima et al with the labeled nucleotides having a disulfide linker (i.e., claims 1 and 10) that is less than 8 atoms (i.e., claim 13) as taught by Urdea et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a method having the added advantage of having a decreased cost as a result of being inexpensively synthesized in large quantity as explicitly taught by Urdea et al (column 2, lines 15-40). In addition, it would have been obvious to the ordinary artisan that the known technique of using the cleavable link of Urdea et al could have been applied to the method of Kawashima et al with predictable results because the Urdea et al predictably results in a link useful in the labeling of nucleotides.

Claims 2-6, 8, and 16, which ultimately depend upon claim 1, would be rejected based on the rejection of claim 1 above and for the reasons set forth in Section 10 of the Final Office Action mailed 10 December 2007.

I. It is noted that page 8 of the Remarks state that claims 1-6, 8-13, and 16 were rejected under 35 USC 103(e), which appears to be a typographical error. The claims were rejected under 35 USC 103(a).

II. Applicant argues on pages 8-9 of the Remarks that Kawashima et al do not teach determining the type of nucleotide and neutralizing a label in each extension step.

However, as stated above, the open claim language "comprising" in line 2 of the claim encompasses additional steps between extension of the primer and the final part of step c) comprising "thereafter determining the type of nucleotide added to the primer and thereafter neutralizing the label

by adding a label-interacting agent or by bleaching repeating steps c) to d) at least once." Thus, after a label is removed by photobleaching (i.e., "step c)" of the instant claims), multiple rounds of enzymatic extension with a mixture of labeled and unlabeled nucleotides and determination of the type of nucleotide added before a subsequent photobleaching step (which constitutes "step d)" of the instant claim) are encompassed by the open claim language "comprising."

C. Claims 11-12, which ultimately depend upon claim 1, would be rejected based on the rejection of claim 1 above and for the reasons set forth in Section 11 of the Final Office Action mailed 10 December 2007.

D. Claim 14, which ultimately depends upon claim 1, would be rejected based on the rejection of claim 1 above and for the reasons set forth in Section 12 of the Final Office Action mailed 10 December 2007.

E. Claim 15, which ultimately depends upon claim 1, would be rejected based on the rejection of claim 1 above and for the reasons set forth in Section 13 of the Final Office Action mailed 10 December 2007.

F. Applicant's remaining arguments on pages 9-10 of the Remarks regarding the rejections under 35 USC 103(a) rely on arguments regarding the alleged deficiencies of Kawashima et al. These arguments are addressed above. Because the arguments were not persuasive, the remaining claims would be rejected based on the rejection of claim 1 above and for the reasons set forth in the Final Office Action mailed 10 December 2007.

G. Applicant further argues on pages 10-11 of the Remarks that the non-statutory obviousness-type double patenting rejections should be withdrawn pursuant to MPEP 804 (I) (B)1.

However, because the claims of the earlier filed instant Application would be rejected under 35 USC 103(a) for the reasons detailed above, the rejections of the claims over claims 33-34 of copending Application 10/529,352 would be **maintained** for the reasons set forth in the previous Office Actions.

Conclusion

4. No claim would be allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571)272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert T. Crow/
Examiner, Art Unit 1634

/Diana B. Johannsen/

Robert T. Crow
Examiner
Art Unit 1634

Art Unit: 1634

Primary Examiner, Art Unit 1634